



UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/601,534	08/28/00	DENNLER	1430-245

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EXAMINER	
TRAN, M	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/601,534

Applicant(s)

DENNLER ET AL.

Examiner

MAU T TRAN

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 March 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 7-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☒ Claim(s) 1-6 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☒ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2.
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

DETAILED ACTION

1. This application is a 371 of PCT EP99/00664 filed on February 4, 1999. Claims 1-21 are pending.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 1-6 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that Yingling et al does not overcome the special technical feature of the instant invention, therefore there is unity of invention. This is not found persuasive because the special technical feature of the instant application is drawn to use of a nucleic acid sequence that is necessary for Smad protein to bind and become activated by TGF-beta which was disclosed by Yingling et al (see specifically last column on page 7021 and figure 3).

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention of Group I, claims 1-6, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10. Claims 1-6 are examined on the merits.

Priority

3. This application filed under former 37 CFR 1.60 lacks the necessary reference to the prior application. A statement reading "This is a 371 of PCT EP99/00664 filed on February 4, 1999, should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included.

4. Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on February 6, 1998. It is noted, however, that applicant has not filed a certified copy of the UK 9802475.5 application as required by 35 U.S.C. 119(b).

Claim Objections

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5. Claims 1-6 are objected to because of the following informalities: The claims have sequences in the claims which have not been properly referred to as SEQ ID Nos. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 recites the term "functional equivalent thereof" without further defining what function to which applicant refers. It is not clear which function applicant is claiming as the instant invention. Further clarification is required. OK

Claim 6 recites "suitable", "hereinbefore defined", "operable linkage" and "detectable" without further defining what these terms are. The terms are used as ~~OK~~ OK relative terminology without further definition to what is being claimed. What is meant by operable linkage? What is detectable and how to detect and what is used to detect? Further clarification is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening agents associated with Smad3/4 and TGF-beta by detecting the activity of said agent between Smad3/4 protein and the oligo sequence consisting of CAGAC, does not reasonably provide enablement for a method of screening agents associated with all Smad proteins and TGF-beta by detecting the activity of the agent between the Smad proteins and the oligo sequence

comprising of CAGAC. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-6 are drawn to a method of screening agents associated with all Smad proteins and TGF-beta by detecting the activity of the agent between the Smad proteins and the oligo sequence comprising of CAGAC and a kit comprising said components. The scope of the claim is not commensurate with what is disclosed in instant application. The nature of the claim is drawn to a method of using the ability of Smad3/4 to become activated upon TGF-beta stimulation and thus bind to the promoter region of genes that contain an oligomer of CAGAC. However, the claim reads on all Smad proteins and all sequences containing the CAGAC oligo. It is clear that not all Smad proteins have the same function as Smad3/4 in this function and are activated by TGF-beta in the same way or function as tumor suppressor proteins (first page, last paragraph of specification).

In addition, the claims also reads on use of said method to treat any and all diseases associated with TGF-beta but there is no teaching or guidance that all diseases are associated with TGF-beta and are also responsive to Smad proteins except certain tumors cells. Moreover, the state of the art and the disclosure of the instant application has not taught how to use the instant invention or to extrapolate the teachings of the instant invention as a treatment for diseases as what was disclosed are in vitro cell culture system and cell extracts with artificial genetic constructs. Applicant is reminded that It is well known in the art that cancer treatment in vivo is a complex process in which the individual's immune response and the host-tumor relationship have to be considered. To assume that all immune systems are alike would be naïve and the pathology, etiology and nature of the disease have to be considered individually (see Osband et al, Immunology Today, 1990, Vol. 11, pg. 193-195, specifically abstract and pg. 193, first column). Therefore, though a drug is able to work in an in vitro environment, it does not necessarily guarantee the success of the therapy *in vivo* or that if the method of treating the cancer would even reach the tumor. The complexities of

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the human body is in no way represented by a petri dish and a cell culture and cannot be assessed without extensive experimentation.

The specification provides insufficient guidance with regard to the issues raised above and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- a. Determining the scope and contents of the prior art.
- b. Ascertaining the differences between the prior art and the claims at issue.
- c. Resolving the level of ordinary skill in the pertinent art.
- d. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yingling et al (cited in previous office action, paper #9).

Claims 1-6 are drawn to a method of screening agents associated with all Smad proteins and TGF-beta by detecting the activity of the agent between the Smad proteins and the oligo sequence comprising of CAGAC and a kit comprising said components. The crux of the invention is using the method of Smad proteins responsiveness to TGF-beta by binding to the CAGAC sequence to screen for drugs.

Yingling et al teaches a method of detecting gene expressing in which cells having the Smad proteins are capable of responding to TGF-beta stimulation by binding to a specific oligo sequence on a reporter gene construct containing specifically the CAGAC sequence and if this sequence is mutated, no gene activation occurs (See especially Figure 3 and Result section). Yingling et al differ from the instant application by not using the disclosed method to screen drugs. However, Yingling also suggests the use of this system to study tumor suppressor effects (last paragraph pg. 7027). Therefore, it would have been *prima facie* obvious for one of the ordinary skill in the art, at the time the invention, was made to use the teachings of Yingling et al to derive at the instant invention with a reasonable expectation of success. One would have been motivated to use the teachings of Yingling et al to derive at the instant invention because it was already known at the time that Smad proteins activate gene transcription by binding specifically to the GACAC site on transcriptional activators and Smad proteins are known to play a role in tumor suppression.

Conclusion

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mau Tran whose telephone number is 703-605-1165. The examiner can normally be reached on Monday-Friday from 8:00 a.m. – 5:30 p.m. with alternate Mondays off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.


GEETHA P. BANSAL
PRIMARY EXAMINER

Mau Tran, Ph.D.

Patent Examiner, Art Unit 1642

April 19, 2001